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## THE TREATMENT OF TETANUS.\*

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This research was undertaken with the object of determining as far as is possible, with animals, the relative value of the various methods of treatment of tetanus.

After a trial of a number of laboratory animals, sheep were selected for the reason that they are susceptible to tetanus, large, and easily handled, they could be bled readily, and because it was possible to infect them in a manner approaching clinical conditions. A 14-day broth culture of a virulent strain of tetanus containing large numbers of bacilli and spores was heated at 65° C. for 20 minutes, for the purpose of destroying the toxin.

In order to be sure of this a part of the material was passed through a Berkefeld and then through a Pasteur filter. One-cubic-centimeter doses of the filtrate thus obtained, when injected subcutaneously into 350-gm. guinea-pigs, failed to produce tetanus. Small pieces of wood were macerated in this toxin-free, spore-containing fluid for two weeks, at the end of which time they were removed and dried.

The method of inoculation was as follows. A sheep with a long tail having been selected, an incision one centimeter in length was made through the skin as near the tip as possible. A pocket was now made by blunt dissection. Into this one piece of infected wood was placed and the wound closed by cat-gut sutures. With the onset of symptoms of tetanus, the tail was amputated 20 cm. above the point of inoculation. No anesthetic was used and antisepsis was observed in all operations.

In order to estimate the amount of toxin present in the blood of the sheep two cubic centimeters were removed at 24-hour intervals and injected into the right hind leg of a 350-gm. guinea-pig. In this way a series of animals was obtained which passed from the normal through the various stages of local and general tetanus to

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the death of animals. Thus a reasonably accurate idea of the amount of toxin present in the blood at the time could be obtained.

For the purpose of studying the effects of amputation, without any other treatment, a series of experiments was undertaken by one of us.<sup>1</sup> Fifty guinea-pigs, 30 dogs, and 10 sheep were used. Immediately on the appearance of symptoms the affected members were amputated. No other treatment was used. Among the conclusions drawn, was the following: "Amputation immediately following the first appearance of symptoms affected in no way the progress of the disease. Animals which were amputated died in the same time and with the same symptoms as those which were not amputated."

From these results, it is reasonable to conclude, therefore, that any benefit obtained by treatment is the result of this treatment and not of amputation.

Having established this point, we undertook the study of the various methods of treatment, as follows: antitetanic serum, carbolic acid method of Bacelli, magnesium sulfate, chlorbutanol alone and in combination with serum.

Six sheep were used in each series, five being treated while one was used as control. In every series, the control animal died with practically identical symptoms in each case.

TABLE I.  
CONTROL SHEEP.

Sheep No.	Series	Inoculated	Symptoms	Amputated	Results
14.....	Carbolic acid	Oct. 29	Nov. 5	Nov. 5	Died Nov. 11
112.....	Magnesium sulfate	March 26	April 4	April 4	" April 6
301.....	Chlorbutanol	July 1	July 8	July 8	" July 12
163.....	Chlorbutanol and serum	" 13	" 20	" 20	" " 24
274.....	Serum	Dec. 13	Dec. 13	Dec. 13	" Dec. 15

#### A SAMPLE PROTOCOL.

Sheep 14, weight 32.6 kilos, control, inoculated as described on October 29, 1909. Sheep appeared normal until 7 days later, when there was noticed a slight stiffening of the front legs when the sheep attempted to run. The neck was held rigid with the nose slightly extended. Eating and drinking were normal. The tail was at once amputated 20 cm. above point of inoculation under antiseptic precautions and the wound closed with cat-gut. Healing of the wound was uneventful.

<sup>1</sup> Hutchings, *Rindfleisch-Festschrift*, p. 601, Leipzig, 1907.

Eighth day: Symptoms were more marked; the sheep walked with some difficulty and fell to knees when attempting to run. Neck stiffer, ate and drank well, chewed cud, and had no difficulty in swallowing.

Ninth day: The sheep remained lying down, but could get up with difficulty. Stiffness pronounced. Ate and drank little. Did not chew cud.

Tenth day: Could not get up alone and when placed on feet could take only a few steps without falling. Ate nothing and swallowed water with difficulty. Stiffness of whole body pronounced.

Eleventh day: Lying on side with head hyper-extended, legs extended and perfectly rigid, could not stand.

Twelfth day: About the same as on the previous day; a few clonic spasms were seen.

Thirteenth day: Clonic spasms frequent but not severe, lasting about 30 seconds. Died during the afternoon.

The following table shows the result of the injection of this sheep's blood into the guinea-pigs.

TABLE 2.

Pig	Weight gm.	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	250	Oct. 30	—	.....	Recovered
2.....	305	" 31	—	.....	"
3.....	275	Nov. 1	+	Nov. 5	"
4.....	290	" 2	+	" 5	"
5.....	308	" 3	+	" 5	Died
6.....	310	" 4	+	" 6	"
7.....	315	" 5	+	" 6	"
8.....	315	" 6	+	" 7	Recovered
9.....	305	" 7	+	" 10	"
10.....	335	" 8	+	" 10	"
11.....	280	" 9	+	" 11	"
12.....	325	" 10	+	" 13	"
13.....	330	" 11	+	" 14	"

From Table 2 it will be seen that measurable amounts of toxin appeared in the blood on the third day, that the toxin was at its maximum from the fifth to the eighth, and persisted until death on the thirteenth day, but that after the eighth day the amount present was small. On the other hand, the clinical symptoms were not discoverable until the seventh day and reached what might be termed a maximum on the eleventh day. Had this train of symptoms appeared in the ordinary case of tetanus in human beings it is probable that the patient would not have come under observation before the eighth day and a diagnosis would not have been reached until the ninth or even the tenth day. From the table one would be inclined to believe that the decrease of toxin in the circulation after the eighth day was a result of the amputation, removal of the source of supply, but that this is not true we have been repeatedly

shown. We have found that the amount of demonstrable toxin in the blood of animals having tetanus, with and without amputation, runs a course practically identical with that shown in the table.

#### SERUM.

Six sheep were used, five treated with intravenous injection of 2,000 units of antitetanic serum every 24 hours, one control. The control died (274). Of those treated four died and one recovered. The protocol of the one that recovered is as follows:

Sheep 108, weight 55.5 kilos.

December 6: Inoculated in tail as usual.

Seventh day: Showed marked stiffness of head and neck. Some stiffness in forelegs, otherwise normal. Tail amputated 20 cm. above point of inoculation. 2,000 units serum injected into left jugular vein.

Eighth day: Somewhat stiffer than day before. Walked with difficulty. While being prepared for bleeding and injection, had several slight clonic spasms and a peculiar "thrill" which is characteristic of tetanus in guinea-pigs. Ate and drank little. 2,000 units serum injected into left jugular vein.

Ninth day: No worse than on previous day. 2,000 units serum injected.

Tenth day: About the same except that he ate and drank better. 2,000 units serum injected.

Eleventh to sixteenth day: Condition remained stationary. 2,000 units of serum were given on each of these days when its use was discontinued. The sheep developed chronic tetanus and was not completely recovered until February 1.

The total amount of serum given was 20,000 units.

TABLE 3.  
RESULTS OF INOCULATION WITH BLOOD OF SHEEP 108.

Pig	Weight gm.	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	350	Dec. 6	—		
2.....	"	" 7	—		
3.....	"	" 8	—		
4.....	"	" 9	—		
5.....	"	" 10	+	Dec. 13	Recovered
6.....	"	" 11	+	" 13	Died
7.....	"	" 12	+	" 14	"
8.....	"	" 13	+	" 16	Recovered
9.....	"	" 14	—		
10.....	"	" 15	—		
11.....	"	" 16	—		
12.....	"	" 17	—		
13.....	"	" 18	—		

The protocol of the sheep which died follows:

Sheep 277, weight 40 kilos.

December 6: Inoculated as usual.

Eighth day: Showed slight stiffness in forelegs, head was slightly extended, otherwise normal. Tail amputated. 2,000 units of serum injected intravenously.

Ninth day: Stiffness increased, drank well but ate little. 2,000 units of serum injected intravenously.

Tenth day: Stiffness very marked, unable to walk but could stand. Refused all food and could not swallow water. Rapid breathing. 2,000 units of serum injected intravenously.

Eleventh day: Very little change from previous day. 2,000 units of serum injected intravenously. Died during the night.

TABLE 4.  
RESULTS OF INJECTIONS WITH BLOOD FROM SHEEP 277.

Pig	Weight gm.	Inoculated with 2 c.c. on	Symptoms	Date	Results
1.....	320	Dec. 5	—		
2.....	300	" 7	—		
3.....	335	" 8	—		
4.....	300	" 9	—		
5.....	250	" 10	+	Dec. 14	Recovered
6.....	255	" 11	+	" 13	Died of tetanus
7.....	330	" 12	+	" 14	" " 17
8.....	330	" 13	+	" 14	" " 18
9.....	325	" 14	+	" 15	" " 18
10.....	325	" 15	—		
11.....	325	" 16	—		
12.....	326	" 17	—		

TABLE 5.  
SHEEP TREATED WITH SERUM ALONE.

Sheep	Inoculated	Symptoms	Amputated	Treatment 2,000 Units	Results
108.....	Dec. 6	Dec. 13	Dec. 13	Serum daily	Recovered
277.....	" 6	" 14	" 14	" "	Died Dec. 18
12.....	" 6	" 12	" 12	" "	" " 18
275.....	" 6	" 14	" 14	" "	" " 18
299.....	" 6	" 14	" 14	" "	" " 22

#### OBSERVATION ON SERUM SHEEP.

1. Twenty-four hours after the first injection of serum, no toxin was found in the blood. This was true of all five sheep.

2. In four of the five sheep, despite the absence of toxin in the blood, the symptoms were not influenced.

#### CARBOLIC ACID.

Before discussing the experiments with sheep it may be of interest to give a few of the preliminary experiments with guinea-pigs. We tried first to determine how much carbolic acid was necessary to kill an average pig.

*Series 1.*—0.5 c.c. of a two per cent solution of carbolic acid in water was injected every two hours until 32 doses were given, without producing any effect. The amount was then increased to one cubic centimeter every two hours. Of this, 11 doses were given before the animals showed symptoms of poisoning.

*Series 2.*—Two other pigs weighing 275 and 256 gm. respectively were given 0.5 c.c. of a two per cent solution until 42 doses were given without producing any effect. Treatment was then discontinued. Ten days later the pigs were alive and in good condition.

*Series 3.*—Five pigs were given 10×M.F.D. of U.S. government standard tetanus toxin. With the first appearance of symptoms they were given 0.5 c.c. of a two per cent carbolic solution every two hours during the day without any apparent effect. All died.

*Series 4.*—Five pigs each received 10×M.F.D. tetanus toxin. The carbolic acid was given every two hours day and night with the result that two pigs recovered and two died.

*Series 5.*—Carbolic injections were begun with two of the pigs immediately after the injection of the toxin with the purpose of determining whether it would prevent the development of tetanus. This it failed to do as the pigs developed the disease and died.

*Sheep treated with carbolic acid.*—Six sheep were used, one as control. Of the sheep treated all received two cubic centimeters of a two per cent carbolic solution every two hours day and night. All died. In comparison with the sheep in which serum alone was used, there was a very slight difference in the tonic muscular contractions, the carbolic sheep being less stiff. The difference, however, was not as marked as with magnesium sulfate and chlorbutanol. It had no influence on the course of the disease.

The following is a sample protocol:

Sheep 17, weight 44.5 kilos.

October 29: Inoculated in the usual way.

Eighth day: Showed stiffness in the front legs, head extended. Stump of tail extended. (This was the only sheep which showed any local tetanus.) Tail amputated 20 cm. above point of inoculation. Two cubic centimeters of a two per cent carbolic solution injected subcutaneously every two hours.

Ninth day: Symptoms more marked. Impossible to get up, but could stand when placed on feet; could not walk without falling. Could not swallow.

Tenth day: Very little change from previous day.

Eleventh day: 10 A.M. clonic convulsions. Died at 8 P.M.

## MAGNESIUM SULFATE.

Our results with magnesium sulfate were unsatisfactory, all of the animals dying either as a result of tetanus or as a result of magnesium sulfate poisoning. Six sheep were used, the control (No. 112) dying of tetanus. Of the five sheep treated, two were given 1.25 gm. per kilo body weight; three were given 2.50 gm. Those receiving the smaller amount showed no effect, while the latter all died apparently of magnesium sulfate poisoning.

## PROTOCOLS.

Sheep 87, weight 35 kilos.

March 26. Inoculated.

Ninth day, 8:30 A.M.: Sheep slightly stiff. Tail amputated, 1.25 gm. magnesium sulfate in salt solution per kilo injected subcutaneously into abdominal wall under aseptic precautions. Fifteen minutes required for injection. During the day the sheep showed no signs of relaxation but became gradually stiffer.

Tenth day: Sheep had well marked tetanus. Unable to get up or stand when placed on feet. Magnesium sulfate repeated, but produced no effect. During the day the sheep became very stiff, legs and neck hyper-extended.

Eleventh day: Dead in stall.

TABLE 6.

Pig	Weight gm.	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	350	March 26	—		
2.....	"	" 27	—		
3.....	"	" 28	—		
4.....	"	" 29	+	April 1	Recovered
5.....	"	" 30	+	" 1	"
6.....	"	" 31	+	" 1	"
7.....	"	April 1	+	" 2	Died
8.....	"	" 2	+	" 3	"
9.....	"	" 3	+	" 4	"
10.....	"	" 4	+	" 5	"
11.....	"	" 5	+	" 6	Recovered

## Protocol of sheep which died from magnesium sulfate poisoning:

Sheep 268, weight 32 kilos.

March 26. Inoculated.

Eighth day: Sheep showed slight signs of stiffness but moved about without difficulty. Tail amputated. 2.5 gm. per kilo of body weight of magnesium sulfate in salt solution injected subcutaneously into abdominal wall under aseptic precautions. At 12:00 the sheep was lying on its side in the stall completely anesthetized. There was relaxation of all muscles. When raised from the floor the animal was quite limp. There was a considerable amount of froth around the mouth and mucous exudate from the nose. Respirations were shallow and infrequent, 12 per minute. This condition was unchanged at 5 P.M.

Ninth day: Sheep dead in stall.



TABLE 7.

Pig	Weight gm.	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	350	March 26	—	.....	.....
2.....	"	" 27	—	.....	.....
3.....	"	" 28	—	.....	.....
4.....	"	" 29	+	April 2	Recovered
5.....	"	" 30	+	" 2	"
6.....	"	" 31	+	" 3	Died
7.....	"	April 1	+	" 3	"
8.....	"	" 2	+	" 3	"
9.....	"	" 3	+	" 4	Recovered

## CHLORBUTANOL.

In administering chlorbutanol to sheep we met with many difficulties. The drug is very slightly soluble in water, 0.8 of one per cent, and somewhat less in normal salt solution. For this reason it was impossible, on account of the amount required, to give it subcutaneously or intravenously. A stomach tube can be passed with little difficulty on a sheep which does not have tetanus. In this way sufficient chlorbutanol can be given in a dilute alcoholic solution. However, when the animal has tetanus, the passage of a stomach tube frequently causes prolonged contraction of the muscles of respiration, leading to death. In our preliminary work several were killed in this way. Chlorbutanol is readily soluble in hot olive oil and remains in solution when the oil is cool. Taking advantage of this fact, we injected chlorbutanol dissolved in oil intraperitoneally. By this method the animals were affected almost as quickly as when the drug was given per stomach. Unfortunately, however, the repeated punctures necessary in a prolonged treatment in many cases cause peritonitis. Altho conducted under aseptic precaution it was not always possible to avoid perforating the gut. In one series we treated the infected animals with chlorbutanol alone and in another with chlorbutanol in combination with serum. The series treated with chlorbutanol alone is as follows:

Six sheep were used, one as control, No. 301. Of these, two died of peritonitis due to the perforation by the injecting needle. One died probably of chlorbutanol poisoning. Two recovered.

The protocols of those dying of peritonitis are not instructive beyond the fact that the muscular symptoms of the tetanus were

entirely controlled and the amount of toxin present in the blood was not affected.

The protocol of the sheep dying of chlorbutanol poisoning is as follows:

Sheep 46, weight 36 kilos.

July 1. Inoculated in usual way.

Seventh day: Sheep slightly stiff, particularly the neck, which he seemed disinclined to move. Tail amputated. Seven grams of chlorbutanol in 100 c.c. of olive oil injected intraperitoneally. One-half hour after injection the sheep was lying on its side apparently asleep. Reflexes, however, were present. Pressure in amputation stump caused slight movement.

Eighth day: In same position and apparently in same condition as day before. Unable to stand and refused to drink.

Ninth day: Sheep lying down but could be easily aroused. Drank a little water with an effort probably due to position. During the day the sheep became wider awake and showed stiffness of forelegs and neck.

5 P.M.: Intraperitoneal injection of 7 grams of chlorbutanol in 100 c.c. of oil.

5:30 P.M.: The animal was completely anesthetized. No eye reflex.

Tenth day: Sheep found in same position as left the night before and dead. Death probably due to chlorbutanol poisoning.

The guinea-pigs injected with blood from this sheep showed the usual results.

The protocols of the two sheep recovering were similar.

Sheep 37, weight 34 kilos.

Inoculated July 1.

Seventh day: Sheep quite stiff. Tail amputated. Intraperitoneal injection of four grams of chlorbutanol in 100 c.c. of olive oil. One hour later the sheep was lying on one side asleep but could be easily aroused. All rigidity of muscles absent. Remained this way during the day.

Eighth day: Sheep lying down but aroused easily. Drank about one-half liter of water. Refused to eat. Four grams of chlorbutanol given intraperitoneally. Sheep remained sleeping during the day.

Ninth day: Sheep in same condition as previous day, not disturbed. No chlorbutanol.

Tenth day: Not moved from position in which he was placed previous day. Drank a small amount of water. No chlorbutanol.

Eleventh day: Sheep awake but unwilling to move. Refused food but drank freely about 1,500 c.c. of water. During the afternoon showed slight return to stiffness.

Twelfth day: Stiffness more marked. Drank water but refused to eat. Four grams of chlorbutanol injected intraperitoneally.

Thirteenth to fifteenth day: Sheep remained quietly sleeping. On the fourteenth day drank a little water. On the morning of the fifteenth day was awake and apparently hungry but could not swallow food. There was no sign of muscular rigidity

From this time the animal continued to drink and on July 17 ate well. There was no sign of the tetanus from this time.

Pigs injected are as follows:

TABLE 8.  
RESULTS OF INOCULATION WITH BLOOD OF SHEEP 37.

Pig	Weight	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	350	July 1	—		
2.....	"	" 2	—		
3.....	"	" 3	—		
4.....	"	" 4	+	July 7	Recovered
5.....	"	" 5	+	" 7	"
6.....	"	" 6	+	" 8	"
7.....	"	" 7	+	" 8	Died
8.....	"	" 8	+	" 9	
9.....	"	" 9	+	" 10	Recovered
10.....	"	" 10	+	" 11	"
11.....	"	" 11	+	" 12	"
12.....	"	" 12	+	" 14	"
13.....	"	" 13	+	" 15	"
14.....	"	" 14	+	" 16	"
15.....	"	" 15	+	" 17	"
16.....	"	" 16	+	" 19	"
17.....	"	" 17	—		
18.....	"	" 18	—		
19.....	"	" 19	—		
20.....	"	" 20	—		

#### CHLORBUTANOL AND SERUM.

Six sheep were used, one as control, No. 163. Of the five treated one died of peritonitis due to perforation. Four recovered.

The protocol of the sheep which died is as follows:

Sheep 300, weight 33.5 kilos.

Inoculated as usual July 13.

Seventh day: Showed slight stiffness in the forelegs. Tail amputated. Five grams of chlorbutanol in 100 c.c. of olive oil injected intraperitoneally and 2,000 units of serum injected intravenously. During the injection the sheep got away from the

TABLE 9.  
RESULTS OF INOCULATION WITH BLOOD OF SHEEP 300.

Pig	Weight	Inoculated with 2 c.c. on	Symptoms	Date	Result
1.....	350	July 13	—		
2.....	"	" 14	—		
3.....	"	" 15	—		
4.....	"	" 16	+	July 18	Recovered
5.....	"	" 17	+	" 19	"
6.....	"	" 18	+	" 19	Died
7.....	"	" 19	+	" 20	"
8.....	"	" 20	+	" 22	Recovered
9.....	"	" 21	—		

attendant and was kept on the table with difficulty. One hour after the injection the sheep was lying on its side asleep. During the afternoon it remained quiet but at 5:30 P.M. abdomen was distended.

Eighth day: Sheep remained quiet but abdomen was greatly distended. 2,000 units of serum injected.

Ninth day: Sheep dead in stall.

Autopsy showed three perforations of the gut, and in the exudate a streptococcus and a long bacillus were found.

TABLE 10.  
RESULTS OF INOCULATIONS WITH BLOOD OF SHEEP 110.

Pig	Weight	Inoculated with 2 c.c. on	Symptoms	Date	Result
1. ....	350	July 13	—		
2. ....	"	" 14	—		
3. ....	"	" 15	—		
4. ....	"	" 16	+	July 18	Recovered
5. ....	"	" 17	+	" 19	"
6. ....	"	" 18	+	" 19	Died
7. ....	"	" 19	+	" 20	"
8. ....	"	" 20	+	" 21	"
9. ....	"	" 21	—		Recovered
10. ....	"	" 22	—		"
11. ....	"	" 23	—		"
12. ....	"	" 24	—		"
13. ....	"	" 25	—		"
14. ....	"	" 26	—		"
15. ....	"	" 27	—		"
16. ....	"	" 28	—		"
17. ....	"	" 29	—		"
18. ....	"	Aug. 30	—		"
19. ....	"	" 1	—		"
20. ....	"	" 5	—		"

The following is a protocol of one of the four sheep which recovered:

Sheep 110, weight 36 kilos.

Inoculated as usual on July 13.

Seventh day: Sheep slightly stiff in forelegs and neck. Tail amputated. Five grams of chlorbutanol injected intraperitoneally and 2,000 units of serum intravenously. One hour later sheep was lying quietly on its side asleep, relaxation complete.

Eighth day: In the same position as previous day, completely relaxed. 2,000 units of serum injected. During the day sheep remained quiet but at 5:30 P.M. began to wake up but refused to drink.

Ninth day: Sheep well awake and slightly stiff. Drank about one liter of water but refused food. Five grams of chlorbutanol in 100 c.c. of olive oil injected intraperitoneally and 2,000 units of serum intravenously. Went to sleep immediately and remained so during the entire day.

Tenth day: In same position as previous day and asleep. No stiffness. 2,000 units of serum injected intravenously.

Eleventh day: Remained lying on side during the day but could be aroused and at 5:30 P.M. drank a little water. 2,000 units of serum. No chlorbutanol.

Twelfth day: Sheep awake and slightly stiff. 2,000 units of serum injected intravenously. During the day the sheep tried to get up but was unable to because of stiffness which had increased to a considerable extent.

5 P.M.: Intraperitoneal injection of 5 grams of chlorbutanol.

Thirteenth to fifteenth day: Sheep remained sleeping quietly. At 5:30 P.M., July 27, could be aroused and drank about 1,500 c.c. of water. On each of these days 2,000 units of serum were given intravenously.

Sixteenth day: Sheep awake but not stiff. During the day remained drowsy but the stiffness did not return as on previous days.

Seventeenth day: Sheep awake, could stand when placed on feet but was very weak. Drank well and ate a small amount.

Eighteenth day: Improved in all conditions. No stiffness and walked a little. Sheep rapidly recovered strength and on August 5 was in normal condition.

The pigs injected were as given in table 10.

#### CONCLUSIONS.

It appears to us that the following conclusions are warranted by these experiments.

1. Amputation after the appearance of symptoms is of no value.
2. The toxin appearing in the blood stream is self-limited even in the fatal cases.
3. There is little if any value in the carbolic acid treatment of the disease.

If there is any gain, our opinion is that it is probably due to the sedative action of the drug and not to any direct action on the disease process, and that this result may be obtained with greater certainty by other drugs.

4. The magnesium sulfate as used in our experiments, subcutaneously, is of no value.

5. Antitetanic serum alone has a definite, altho usually insufficient curative effect.

6. It appears to us, from the observation of a large number of animals and quite a number of human beings dying of tetanus, that the exhaustion due to the muscular contractions is a large factor in producing fatal results. For this reason much of our work has been given to the attempt to hold these convulsions in check.

7. The presence of a large amount of toxin in the blood several days (in sheep it can be demonstrated four days) before the onset of clinical symptoms makes it imperative that a method be devised for easily determining this. With such a method it is quite probable that we could save a large proportion of our tetanus cases.

8. With our present knowledge of the subject, the best that can be done in the treatment of tetanus is to neutralize the toxin with repeated doses of serum while controlling the muscular spasm with some such drug as chlorbutanol.